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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,019	10/20/2003	Jeremy Nathans	JHU1380-2	5064

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
12/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,019	NATHANS ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-37 and 40-47* is/are pending in the application.

4a) Of the above claim(s) *21-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20 and 40-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10-13-08 has been entered.

Claims 19-37 and 40-47 are pending. Claims 19, 20 and 40-47 are under examination. Claims 21-37 are withdrawn from consideration.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

Claims 19, 20 and 40-45 stand rejected under 35 U.S.C. 102(e) as being clearly anticipated by Greene et al (US Patent No. 6,482,408, with priority to June 5, 1995) is withdrawn in view of Applicants amendments to the claims.

Claims 19, 20, 38 and 40-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Hu et al (U.S. Patent 5,817,485, issued October 6, 1998, with priority to March 8, 1994) is withdrawn in view of Applicants amendments to the claims.

Claims 19, 20 and 40-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greene et al (US Patent No. 6,482,408, with priority to June 5, 1995) in view of Harlow et al, (Antibodies A Laboratory Manual, 1989, Cold Spring Harbor Laboratory,

Chapter 9, pages 319-358) and Nathans et al (5,872,226, with priority to May 12, 1995) is withdrawn in view of Applicants amendments to the claims.

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 20 and 40-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated antibody that specifically binds to polypeptide consisting of amino acids 1-65 of SEQ IDNO:4. The specification generically contemplates fragments of the FHF polypeptides that retain at least one FHF-specific activity or epitope (page 12, lines 23-24). The specification generically contemplates fragments that are conserved in FHF's but not FGFs (see paragraph bridging pages 12-13). The specification generically contemplates monoclonal and polyclonal antibodies that specifically bind to FHF poypeptides and the use of PFH polypeptide fragments as antigens to make the antibodies (see page 23, lines 14-25).

The specification does not teach the polypeptide consisting of residues 1-65 of SEQ ID NO:4 retains at least one FHF-specific activity or epitope. The specification

generically contemplates fragments of FHF polypeptides of at least 8-10 amino acids but does not explicitly or inherently use or point to any polypeptide fragment consisting of the indicated residues for making an antibody or for any other disclosed purpose. Residues 1-65 of SEQ ID NO:4 is not characterized in the specification as having at least one FHF-specific activity. Furthermore, the specification does not teach or characterize the epitopes present on the FHF-4 (SEQ ID NO:4). Therefore, while the specification discloses the sequence of the FHF-4 antigen as SEQ ID NO:4, it does not disclose what fragments of the sequence comprise epitopes and does not lead the skilled artisan to residues 1-65 as being of any particular importance. The art recognizes that defining epitopes is not as easy as it seems (Greenspan et al. (Nature Biotechnology 7: 936-937, 1999). Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contact with a ligand but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the epitopes (of an antigen) that can elicit an antibody response to a given polypeptide can only be identified empirically. While the art can conventionally scan for ***potential*** contiguous antibody epitopes using conventional art accepted algorithms (Greenbaum et al, Journal of Molecular Recognition, 20(2):75-82, 2007), these methods do not identify discontinuous epitopes which are identified by crystallization of antibody/antigen complexes. The quality of the methods for B cell epitope prediction was widely considered to be too poor to be employed as a reliable tool by immunologists (paragraph spanning pages 75-82). The art recognizes that defining epitopes is not easy and there is a confusing divergence between the textbook definition of epitope and the definition that is in use in published descriptions of experimental investigations (Greenspan et al, Nature Biotechnology 17:936-937, 1999). The

specification clearly lacks description of any particular epitope (i.e. antigenic determinant), either continuous or discontinuous that for either a T cell or B cell. Even as late as 2005 the art recognized that single-scale amino acid propensity profiles could not be used to predict epitope location reliably (Blythe et al, Protein Science 14:246-248, 2005). As such, disclosure of the primary sequence *per se*, does not place the B cell epitopes within in possession of the skilled artisan.

In considering sufficiency of support in specification for specific compound, specification must be looked at from standpoint of one with no foreknowledge of compound; while person motivated to make compound in preference to others would be enabled by specification to make it, this is beside the point for question is not whether he/she would be so enabled, but whether specification disclosed the compound to him/her, specifically as something applicant invented. *In re Ruschig* 154 USPQ 118 (CCPA 1967). The written description requirement ensures that, at the time a patent application is filed, the inventor has possession of the invention claimed. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). It also serves the obvious purpose of telling the public what it is that has been invented. Possession of the invention at the time of filing is best shown by a precise description in the text of the patent specification of all of the aspects of the claimed invention. It is true that a patent need not describe the claimed subject matter in precisely the same terms as used in the claims, see *Vas-Cath*, 19 USPQ2d at 1116; however, it must still describe the invention with all its claimed limitations in some manner, see *Lockwood v. American Airlines, Inc.* , 1 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Wertheim*, 191 USPQ 90, 96 (CCPA 1979). "Precisely how close the original description must come to comply with Section 112 must be left to case-by-case development." *Vas-Cath*, 19 USPQ2d at 1116 (citing *In re Smith*, 173 USPQ 679, 683 (CCPA 1972)). If the written description does not use precisely the same terms used in a claim, the question then is whether the specification directs or guides one skilled in the art to the subject matter claimed. See, e.g., *Fujikawa v. Wattanasin*, 39 USPQ2d 1895,

1904 (Fed. Cir. 1996). It has been analogized that the requirement that the written description direct one to the claimed subject matter to "blaze marks" on specific trees that mark a trail through a forest. See *In re Ruschig*, 154 USPQ 118, 122 (CCPA 1967). It has been found that without such specific direction, a general disclosure will not be sufficient to support narrowly claimed subject matter. See *Fujikawa v. Wattanasi*, 39 USPQ2d 1895, 1905 (CAFC 1996).

In the instant case, there is nothing described or provided in the specification or figures to direct to the skilled artisan to residues 1-65 of SEQ ID NO:4 or antibodies that specifically bind thereto.

Status of Claims

Claims 19, 20 and 40-47 stand rejected. Claims 21-37 are withdrawn from consideration.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 7:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisors, Robert Mondesi can be reached at 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/
Primary Examiner